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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/039,177      | 03/13/1998  | KOHEI MIYAZONO       | LUD-5539            | 9274             |

24972 7590 12/03/2001  
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EXAMINER

ROMEO, DAVID S

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1647

DATE MAILED: 12/03/2001

*24*

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/039,177

Applicant(s)

MIYAZONO ET AL.

Examiner

David S Romeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-20,25,27 and 29-31 is/are pending in the application.
- 4a) Of the above claim(s) 1-20,25 and 27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 29-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-20,25,27 and 29-31 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_. 6) ☒ Other: See Continuation Sheet.

Continuation of Attachment(s) 6). Other: Notice to Comply; and, Raw Sequence Listing Error Report.

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**DETAILED ACTION**

1. The amendment filed 09/21/2001 (Paper No. 23) has been entered. Claims 1-20, 25, 27, 29-31 are pending. Claims 1-20, 25, 27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as drawn to non-elected inventions. Claims 29-31 are being  
5 examined. Any objection or rejection of record that is not maintained in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The communication filed 09/21/2001 is not fully responsive to the Office communication mailed 07/31/2000 (Paper No. 15) for the reason(s) set forth on the attached Notice To Comply  
10 With The Sequence Rules and Raw Sequence Listing Error Report.

Correction is required.

3. Applicants' arguments have been fully considered but they are moot in view of the new grounds of rejection that follow.

**New formal matters, objections, and/or rejections:**

***Claim Rejections - 35 USC § 112***

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4. Claims 29-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification teaches that ALK-1 binds TGF- $\beta$ 1 and activin A but the functional consequences of this binding remain to be elucidated (sentence bridging pages 33-34); ALK-1 is a receptor for TGF- $\beta$  (page 35, lines 7-8); a constitutively active form of ALK-1 phosphorylated Smad1 (paragraph bridging pages 35-36); and, TGF- $\beta$  binds to ALK-1 leading to phosphorylation of Smad1 (page 37, lines 6-7). In view of the disclosure that ALK-1 binds TGF- $\beta$ 1 and activin A but the functional consequences of this binding remain to be elucidated (sentence bridging pages 33-34) the specification manifestly fails to describe the enhancement of gene expression.

5. The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 29 is indefinite over the recitation of "TGF- $\beta$  which activates phosphorylation of Smad1" because it is unclear if the "contacting" "activates phosphorylation of Smad1" or if TGF- $\beta$  is just a molecule that happens to activate "phosphorylation of Smad1"

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irrespective of the "contacting". The antecedent basis for this limitation is unclear. The metes and bounds of the claim(s) are not clearly set forth.

b. Claims 29, 30 are indefinite because they lack a process step which clearly relates back to the claim preamble and it is unclear what process is to be achieved; an intended use is not the same as achieving a result; in the absence of a recitation as to any result, or a process step producing a result, it is unclear what result of the process can be inferred. It is suggested that the claims recite "and enhance expression of a gene" after "Smad1" at the end of the claim.

*Claim Rejections - 35 USC § 102*

6. Claims 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki (u24)<sup>1</sup> in view/light of Ying (v24). Suzuki teaches a method of enhancing the expression of ICAM-1 comprising contacting HUVECs with TGF- $\beta$ , removing transcripts from said HUVECs, and comparing said transcripts to transcripts from HUVECs not treated with TGF- $\beta$  (page 1282, column 1, full paragraph 3; Figure 2). HUVECs are cells which express ALK-1, according to the instant specification at page 35, full paragraph 2. The specification at page 37, lines 6-7, also teaches that TGF- $\beta$  binds to ALK-1 leading to phosphorylation of Smad1, which indicates that

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<sup>1</sup>Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

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contacting HUVECs with TGF- $\beta$  phosphorylates Smad1 in the absence of evidence to the contrary. Ying teaches that Smad1 transcripts were mainly detected in vascular endothelial cells (Abstract), indicating that HUVECs express Smad1 in the absence of evidence to the contrary. The TGF- $\beta$  used by Suzuki is a portion of TGF- $\beta$  sufficient to bind ALK-1 and activate phosphorylation of ALK-1.

**Conclusion**


7. No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

OFFICIAL PAPERS FILED BY FAX SHOULD BE DIRECTED TO (703) 308-4242.

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294. ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

  
DAVID ROMEO  
PRIMARY EXAMINER  
ART UNIT 1647

NOVEMBER 27, 2001